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First Night Effects in Post-Traumatic Stress Disorder Inpatients

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Summary: Recent data have suggested that first night effects are attenuated in inpatient depressive subjects. We examined first night effects in 80 inpatients hospitalized for post-traumatic stress disorder (PTSD) as well as non-hospitalized PTSD sufferers and non-ill control subjects. PTSD inpatients exhibited attenuated first night effects compared to non-hospitalized PTSD sufferers and non-trauma-exposed controls. Non-ill combat-exposed subjects also exhibited small first night effects. Within the inpatient sample, severity indices of PTSD, depression and anxiety failed to account for variance in first night effects. These data demonstrate attenuation of first night effects in a new inpatient population and suggest their statistical independence vis-à-vis a range of relevant symptoms. Both the attenuation of first night effects in PTSD inpatients and their accentuation in PTSD outpatients may be indicative of enhanced sensitivity to the sleep environment. Conversely, the trend to small first night effects in non-ill combat-exposed subjects may reflect a dimension of their apparent resistance to traumatic stress. **Key Words:** Sleep—PTSD—First night effects.

Disturbances of sleep observed on the first night of a multi-night sleep study relative to later nights are labeled first night effects (FNEs) (1–5). The sleep parameters most reliably demonstrating FNEs are sleep efficiency, sleep onset latency and rapid eye movement (REM) percent of sleep. In view of FNEs, it has been standard practice among sleep researchers to dispose of the first night of laboratory data. Given the preponderance of 2- and 3-night studies in the sleep literature (especially those with large samples), it is reasonable to conclude that a substantial fraction (~25%) of all human sleep data collected in the course of subsequently published work has been so excluded. Toussaint et al. (5) recently reported that a sample of inpatient depressive subjects (n = 36) failed to demonstrate significant FNEs in sleep efficiency, sleep onset latency or REM percent of sleep [FNEs were observed in REM latency and a non-rapid eye movement (NREM)/REM percentage measure]. An earlier study by Reynolds et al. (6), comparing nights 1 and 2 in closely matched inpatient and outpatient depressive samples, also found reduced first night effects in inpatients. These authors remarked that the inpatients appeared "locked in . . . to a given organization of sleep" (6). Both groups of authors (5,6) suggested that differences in familiarity with the sleep environment could have accounted for differences in adaptation.

FNEs in gross sleep architecture have not been examined in post-traumatic stress disorder (PTSD). PTSD patients represent an interesting test population in regards to the question of FNE attenuation in inpatient samples. In many settings, PTSD patients demonstrate high levels of vigilance, environmental sensitivity and paranoid cognition, propensities one might expect to translate into enhanced FNEs. On the other hand, PTSD-related nightmares are only rarely observed in the sleep laboratory, suggesting that some ameliorative effect upon sleep may be established by the secure and "guarded" environment. It is difficult to extrapolate a prediction regarding FNEs in PTSD from published data obtained from anxious and depressed outpatient samples. Akiskal et al. (7) reported that anxious depressive subjects exhibited enhanced FNEs for sleep continuity parameters. Kupfer et al. (8) found enhanced FNEs in young depressive subjects in NREM sleep parameters. In contrast, Goetz et al. (9)

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reported that young endogenous depressive subjects demonstrated reduced FNEs in NREM sleep parameters, and Coble et al. (2) observed reduced FNEs for REM sleep latency in depressed patients. Reynolds et al. (10) reported that generalized anxiety disorder and depressed patients exhibited differential FNEs, with the former exhibiting FNEs in NREM and sleep continuity parameters and the latter exhibiting FNEs in REM parameters. Thus, there is no clear pattern of association between FNEs and the psychiatric diagnoses most closely related to PTSD.

MATERIALS AND METHODS

Subjects

Inpatient subjects were recruited from the Specialized Inpatient PTSD Unit at the Department of Veterans Affairs Medical Center (DVAMC), Palo Alto (Menlo Park Division). All were free of psychotropic medication at the time of study. If medicated prior to study (15% of subjects), they had undergone drug washout periods equal to or greater than four half-lives. Outpatient and non-ill control subjects were recruited via flyers in the medical center and local newspaper advertisements. Potential subjects were excluded if they reported obvious indications of obstructive sleep apnea or histories of central nervous system disease. Potential subjects were also excluded if they reported having undergone a 30-day period of daily alcohol intake exceeding 5 ounces per day at any time during the prior 6 months or (if outpatients) they would not agree to refrain from alcohol use for 2 weeks prior to the study. All subjects were administered the Structured Clinical Interview for the DSM-III-R (11) and the Clinician Administered PTSD Scale (CAPS) (12) (the CAPS version assessed DSM-III-R rather than DSM-IV criteria for PTSD; however, in this sample, the likelihood that any subjects would be reclassified as not having current PTSD using DSM-IV is remote). All inpatient subjects were also interviewed by a psychiatrist experienced in the diagnosis of PTSD. For males, PTSD, if present, was secondary to combat trauma suffered during the Vietnam War. For females, PTSD was typically secondary to war-related experiences or to physical or sexual assault(s) sustained during military service. Many PTSD subjects also met criteria for one or more comorbid diagnosis [major depressive disorder, substance abuse/dependence (in remission), panic disorder, agoraphobia without history of panic disorder]. Data from tested subjects were excluded from further analysis if there was objective evidence of sleep apnea on any laboratory night.

Sleep data were evaluated over four groups of subjects: PTSD inpatients (n = 80), non-hospitalized PTSD sufferers ("PTSD outpatients", n = 7), combat-exposed persons without histories of mental illness ("non-ill combat-exposed", n = 6), and non-trauma-exposed individuals without histories of mental illness ("non-ill trauma-free", n = 8). The groups were very closely matched in age (46, 45, 48 and 44 years, respectively). Containing four, zero, zero and two women, respectively, the groups also did not differ significantly in gender composition [$\chi^2(4) = 5.788$, $p = 0.216$].

Procedures

Subjects scheduled their own sleep within the constraints imposed by the inpatient treatment program. The latter operated most strongly upon arousal times, because mandatory breakfast was scheduled at 6:30 a.m. Bedtimes were to some degree constrained by technician scheduling and hookup time to be later than 9:00 p.m., although patients rarely requested such early bedtimes. Patients could also get out of bed at any time to use the bathroom. The recording montage included two channels of bipolar electrooculogram (EOG) and four channels of scalp electroencephalogram (EEG) (F3, F4, CZ and Pz, referred to linked mastoids and filtered to a bandwidth of 0.3–30 Hz). Electromyogram (EMG) was recorded from mental and left anterior tibial sites and filtered to a bandwidth of 10–100 Hz. Electrocardiogram (ECG), respiratory effort and blood oxygen saturation were also recorded. Manual sleep stage scoring was performed following the Rechtschaffen and Kales (13) criteria, applied to 30-second epochs.

RESULTS

Between-group analyses

First-night and post-adaptational sleep architecture parameters are presented adjacent to one another in Table 1. An omnibus repeated-measures analysis of variance (ANOVA) was calculated. Overall, there was a nearly significant main effect of group on sleep architecture [$F(3, 97) = 2.328$, $p = 0.079$] and a group by (sleep architecture) parameter interaction [$F(21, 679) = 4.32$, $p < 0.001$]. Decomposing the latter, we found significant effects of group upon sleep efficiency [$F(3, 97) = 3.882$, $p = 0.011$], REM percentage [$F(3, 97) = 4.614$, $p = 0.005$) and time asleep [$F(3, 97) = 5.519$, $p = 0.002$] but on no other sleep architecture parameters tested. We will defer further analysis of these effects until adaptation effects have been described.

There was a main effect of adaptation [$F(1, 97) =$

TABLE 1. *Sleep architecture on night 1 and post-adaptational nights*

		Sleep efficiency		Sleep latency		REM percentage		REM latency	
Group	n	1st	Post	1st	Post	1st	Post	1st	Post
PTSD inpatients	80	89.7	91.55	7.2	7.01	24.8	26.53	76.8	65.55
		6.2	4.81	5.3	5.39	7.2	5.69	32.2	27.21
PTSD outpatients	7	78.1	91.17	15.1	7.69	16.5	23.28	98.7	66.9
		11.9	2.94	11.9	4.26	10.5	5.63	80	27.93
Non-ill combat-exposed	6	90.9	92.2	6.9	5.9	21.6	23.7	65.3	76.2
		5	4.4	6.5	3.6	7.2	3.9	49.1	12.7
Non-ill non-trauma-exposed	8	84.4	91.4	11.9	8.6	16.9	22.8	91.5	75.3
		8.2	5.1	8.5	5.3	7.3	7.5	46.2	16.3
Between-group F-ratio (3, 97)		7.598	0.058	4.45	0.546	5.059	1.882	1.204	0.602
p-value		0.001	ns	0.006	ns	0.003	ns	ns	ns
FNE F-ratio (1, 97)		33.4		9.744		12.599		3.716	
p-value		0.001		0.002		0.001		ns	
FNE × group F-ratio (3, 97)		8.994		3.412		1.845		1.435	
p-value		0.001		0.021		ns		ns	
FNE × group 1 df contrasts									
F-ratio (1, 97)		1 vs. 2	23.786	1 vs. 2	9.08				
p-value			0.001		0.003				
		1 vs. 4	26.491	1 vs. 4	4.955				
			0.001		0.028				
		2 vs. 3	22.679	2 vs. 3	8.921				
			0.001		0.004				
		3 vs. 4	12.503						
			0.001						

1st indicates night 1; Post indicates post-adaptational nights; ns = not significant; df = degrees of freedom. Standard deviations are printed below corresponding means.

11.429, p = 0.001) and no overall group by adaptation interaction [$F(3, 97) = 1.455$, p = 0.232] but a significant group by adaptation by parameter interaction [$F(8, 582) = 2.995$, $p < 0.006$, $\epsilon = 0.3732$; Huynh-Feldt corrections for non-sphericity were employed, and Huynh-Feldt epsilon was reported]. Sleep architecture parameters demonstrating significant adaptation were sleep efficiency [$F(3, 97) = 33.4$, $p < 0.001$], sleep latency [$F(3, 97) = 9.744$, $p < 0.002$], REM percentage [$F(3, 97) = 12.599$, $p < 0.001$], time asleep [$F(3, 97) = 30.29$, $p < 0.001$] and stage 1 sleep percentage [$F(3, 97) = 4.16$, $p < 0.044$]. All adaptation effects were in the expected direction. Sleep architecture parameters demonstrating significant differences in adaptation over groups were sleep efficiency [$F(3, 97) = 8.994$, $p < 0.001$], sleep onset latency [$F(3, 97) = 3.412$, p = 0.021] and time asleep [$F(3, 97) = 3.836$, p = 0.012]. As can be discerned from Table 1, the consequence of significant group differences in adaptation for sleep efficiency, sleep latency and time asleep was that univariate effects of group were significant when these parameters were extracted from night 1 but not when they were extracted from post-adaptational sleep. The pattern for REM percentage was somewhat different in that the adaptation of REM percentage did not differ over groups [$F(3, 97) = 1.845$, p = 0.144] and so would not appear to undermine the effect of group; however, Table 1 again demonstrates that univariate effects of group were significant for REM percentage on night 1 only. Insofar as all significant group by parameter interactions were subsumed by group by adaptation by parameter interactions, and there were no significant effects of group upon parameters extracted from post-adaptational sleep, further decomposition of the group by parameter interactions was not indicated. Decomposition of the group by adaptation by parameter interactions (on sleep efficiency, sleep latency and time asleep) demonstrated that PTSD inpatients were consistently different from both PTSD outpatients and from trauma-free control subjects (see Table 1).

Analyses within PTSD inpatients

In the context of FNEs, the adaptational increase in REM sleep percentage that is generally observed is interesting in that, unlike increases in sleep efficiency and reductions in sleep latency, it is not unambiguously associated with improved sleep. We examined two likely predictors of adaptation in REM sleep percentage within the PTSD inpatient subsample: adaptation in REM latency (indexing variability in REM onset) and in arousal time (indexing completion of the late REM-rich periods of sleep). In these and similar analyses below, adaptation was indexed by the difference between night 1 and post-adaptational sleep for

TABLE 1. *Continued*

Time asleep		Stage 1 percentage		Stage 2 percentage		Slow ware percentage	
1st	Post	1st	Post	1st	Post	1st	Post
325.4	346.4	13.2	11.09	54	53.48	7.9	8.9
51.6	48.17	6	4.66	10.3	9.77	8.9	9.01
230.4	308	15.4	12.09	58.2	58.24	9.9	6.37
32.1	65.48	10.2	4.05	15.4	5.57	10.7	6.88
301.9	332.2	13.4	15.1	56	51.5	9.1	9.8
47.7	57	7.4	8.1	6.9	4.9	7.7	6.7
294.8	322.4	14.5	10.1	52	50.4	16.5	16.7
37.2	39.4	6.2	10.7	8.4	10.7	11.9	13.4
8.595	1.805	0.807	1.431	0.519	0.965	2.134	2.028
0.001	ns	ns	ns	ns	ns	ns	ns
30.29		4.16		0.185		0.162	
0.001		0.044		ns		ns	
3.836		1.279		0.598		1.235	
0.012		ns		ns		ns	
1 vs. 2	16.21						
	0.001						
1 vs. 4	11.39						
	0.001						
2 vs. 3	11.43						
	0.001						
3 vs. 4	4.015						
	0.048						

tested parameters. Only adaptation in REM latency significantly predicted adaptation in REM sleep percentage, accounting for 42% of the variance. This observation suggested that adaptation in REM sleep percentage might be secondary to changes in sleep initiation. In order to test whether changes in sleep initiation might also best account for changes in time asleep, we compared the predictive powers of sleep latency and arousal time. In contrast, adaptation in arousal times accounted for 15% of the variance in adaptation in time asleep. Only a negligible portion was accounted for by adaptation of sleep latency.

For most members (n = 79) of the PTSD inpatient sample, we had psychometric data obtained upon admission to the inpatient program (35 days, on average, prior to testing). These measures, the Beck Depression Inventory (BDI) (14), the Beck Anxiety Inventory (BAI) (15) and the Mississippi Scale of Combat-Related PTSD (MISS) (16) index psychiatric symptoms related to mood disorders frequently addressed in sleep studies, such as depression and anxiety, and potentially related to sleep laboratory adaptation in PTSD. None of these indices, alone or in combination, accounted for significant variance in adaptation of sleep efficiency, sleep latency, time asleep, REM sleep percentage or REM latency. The absence of correlations was not due to range restriction in FNE magnitudes.

Finally, we considered whether the familiarity of patients with the general hospital/ward environment, as indexed by the length of hospitalization in days prior to testing, covaried with their adaptation to the sleep laboratory. Table 2 presents product-moment correlations between inpatient days prior to testing and FNE magnitudes. [Two patients with lengths of hospitalization prior to testing that were more than two standard deviations (SDs) away from the mean, i.e. longer than 135 days, were excluded from this analysis.] The pattern of correlations suggested that PTSD inpatients who had resided in the hospital longer prior to testing tended to show larger adaptation effects in the direction of higher stage REM percentages on post-adaptational nights ($r = -0.258$, $p = 0.022$). This effect is plotted in Fig. 1. Correlations involving sleep efficiency, sleep latency, time asleep and REM latency were insignificant. Finally, we tested the ability of inpatient days to account for variance in REM sleep percentage after variance accounted for by adaptation in REM latency and by the psychometric indices was removed.

TABLE 2. *Pearson product-moment correlations between length of hospitalization prior to sleep testing and FNE difference-score magnitudes for selected sleep architectural parameters*

	Days inpatient before testing	Sleep efficiency	Sleep latency	Time asleep	REM sleep percentage
Sleep efficiency	−0.012				
Sleep latency	−0.189	***−0.373***			
Time asleep	−0.039	**0.351**	0.038		
REM sleep percentage	*−0.258*	−0.034	*0.243*	−0.12	
REM latency	0.121	−0.014	*−0.243*	0.075	***−0.633***

Coefficients in italics exceed an alpha level of 0.05, those in bold exceed an alpha level of 0.01 and those both italic and bold exceed a level of 0.001. Two patients with abnormal lengths of hospitalization prior to testing (>130 days) were excluded from this analysis (n = 78).

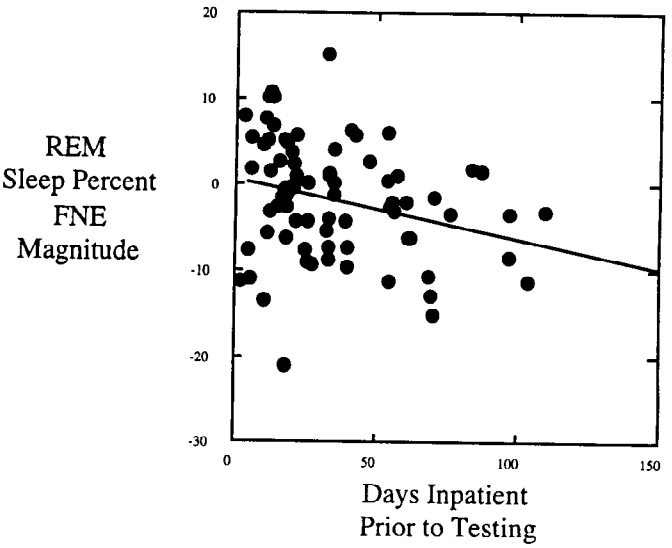

FIG. 1. REM sleep percentage FNE difference-score magnitude plotted against length of hospitalization prior to sleep testing.

Under these conditions, the proportion of variance in REM percentage adaptation accounted for by inpatients days was reduced, but it remained nearly significant ($p = 0.07$).

DISCUSSION

These data confirm and extend the findings of Toussaint et al. (5) and Reynolds et al. (6) by demonstrating the attenuation of FNEs of inpatients in another diagnosis, PTSD. The observation of preserved FNEs in PTSD outpatients demonstrated that some factor associated with inpatient status, per se, rather than PTSD, was the likely source of FNE attenuation. FNEs of non-ill trauma-free controls were intermediate between PTSD inpatients and outpatients, whereas those of non-ill combat-exposed control subjects were also small. The possibility that familiarity with the sleep environment resulted in reduced FNEs in inpatients is consistent with the observation of reduced or absent FNEs in subjects tested in their homes using ambulatory monitoring technology (4). A parsimonious explanation for the pattern of findings observed is that PTSD patients were bidirectionally sensitive to the degree of familiarity they associated with the sleep laboratory. That is, inpatients familiar with the laboratory environment demonstrated reduced FNEs, whereas PTSD sufferers unfamiliar with the environment demonstrated enhanced FNEs. Non-ill trauma-free subjects produced FNEs intermediate between PTSD inpatients and outpatients. The non-ill combat-exposed subjects provide an interesting amendment to this pattern; the fact that their sleep (as indexed by sleep efficiency, sleep latency and REM sleep percentage) was negligibly influenced by the unfamiliarity of the sleep laboratory may index a dimension of their resistance to traumatic stress. Whether a stabile sleep pattern is a primary or secondary feature of such resistance is an open question. Wang et al. (17), in considering the dynamics of chronic PTSD, suggested that erosions in sleep quality typically precede, and perhaps play a causative role in, the repeated decompensations characteristic of the disorder.

The availability of a large and variably symptomatic sample of PTSD inpatients allowed us to test whether severities in depressive, anxious and/or PTSD symptoms were related to laboratory adaptation in gross sleep architecture. They were not. A weak relationship was observed between length of hospitalization prior to testing and REM sleep percentage FNE magnitude. This could be interpreted as supporting the between-group findings suggesting that familiarity with the hospital environment reduces sleep laboratory adaptation. Not clear is how the intercept and directionality of the relationship should be interpreted, because within the inpatient group, those with shorter than median hospitalizations showed near-zero FNEs in REM percentage whereas those with greater than median hospitalizations demonstrated non-zero adaptation in the direction of more REM sleep on post-adaptational nights (see Fig 1). In light of this question, the inherent weakness of the relationship, and the fact that no other sleep architecture parameter tested demonstrated a relationship between length of hospitalization and FNE magnitude, we should interpret the observation cautiously. Within the limitations of the parameters and indices tested here the data suggest that the FNEs of inpatient PTSD subjects are small and nonsystematic. Such results, along with those of Toussaint et al. (5), and Reynolds et al (6), support the retention of night 1 data in sleep studies performed on inpatient psychiatric samples.

Finally, the major portion of the adaptational change in REM sleep percentage was accounted for by changes in REM latency, a process occurring during the first 100 minutes of sleep. It was not well accounted for by changes in arousal time, even though the late sleep period usually contains abundant REM sleep. In contrast, changes in arousal time, rather than sleep latency, accounted for changes in time asleep. Together these observations suggest multiple adaptational processes that are at least partially separable.

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